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<p>Substitute for form 1449A/B/PTO</p> <p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b></p> <p><i>(Use as many sheets as necessary)</i></p>				<i>Complete if Known</i>	
				Application Number	10/658745
				Filing Date	September 8, 2003
				First Named Inventor	Linda Burkly
				Art Unit	<del>1641</del> 1649
				Examiner Name	Not Yet Assigned BRAUNACK
Sheet	1	of	1	Attorney Docket Number	CIBT-P02-115

U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document Country Code <sup>3</sup> -Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
WJ	BA	WO 98/30576	07-16-1998	The Johns Hopkins University School of Medicine	T <sup>6</sup>

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. <sup>6</sup>Applicant is to place a check mark here if English language Translation is attached.

NON PATENT LITERATURE DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.			
AM	CA	Porter, J. A. et al., "Cholesterol Modification of Hedgehog Signaling Proteins in Animal Development", Science Vol. 274, Issue 5285, pp. 255-259 (1996).			

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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Examiner Signature 9659427_1	<i>Marie</i>	Date Considered	10/17/06
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9/8/2003

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Form PTO-1449 <b>INFORMATION DISCLOSURE CITATION IN AN APPLICATION</b> <i>(Use several sheets if necessary)</i>	Docket Number (Optional) CIBT-P02-115		Application Number <u>10/658,745</u>
	Applicant Burkly and Wang		
	Filing Date September 8, 2003		Group Art Unit <u>1649</u>

**U.S. PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
WJ	AA 5,798,230	8/25/98	Bornkamm et al			
	AB 5,789,650	8/4/98	Lonberg et al.			
	AC 5,759,811	6/2/98	Epstein et al.			
	AD 5,747,641	5/5/98	Frankel et al.			
	AE 5,328,470	7/12/94	Nabel et al.			
	AF 5,223,409	6/29/93	Ladner et al.			
	AG 5,198,346	3/30/93	Ladner et al.			
	AH 5,122,464	6/16/92	Wilson et al.			
	AI 5,096,815	3/17/92	Ladner et al.			
	AJ 4,980,286	12/25/90	Morgan et al.			
	AK 4,874,702	10/17/89	Fiers et al.			
	AL 4,868,116	9/19/89	Morgan et al.			
WJ	AM 4,588,585	5/13/86	Mark et al.			

**FOREIGN PATENT DOCUMENTS**

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	Translation	
						YES	NO
WJ	AN WO 95/23223	8/31/95	PCT				
	AO WO 95/18856	7/13/95	PCT				
	AP WO 92/09690	6/11/92	PCT				
	AQ WO 92/07573	5/14/92	PCT				
	AR WO 91/06309	5/16/91	PCT				
	AS WO 90/07861	7/26/90	PCT				
	AT WO 89/07136	8/10/89	PCT				
	AU WO 89/05345	6/15/89	PCT				
	AV WO 89/02468	3/23/89	PCT				
	AW WO 88/06630	9/7/88	PCT				
WJ	AX EP 412762	2/13/91	EPC				

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Form PTO-1449 <b>INFORMATION DISCLOSURE</b> <b>CITATION</b> <b>IN AN APPLICATION</b> <i>(Use several sheets if necessary)</i>		Docket Number (Optional) CIBT-P02-115	Application Number
		Applicant Burkly and Wang	
		Filing Date September 8, 2003	Group Art Unit
<b>OTHER DOCUMENTS</b> <i>(Including Author, Title, Date, Pertinent Pages Etc.)</i>			
W/	AY	Agterberg et al., 1990, "Outer-membrane PhoE protein of Escherichia coli K-12 as an exposure vector: possibilities and limitations", Gene 88:37-45	
	AZ	Apelqvist et al., 1997, "Sonic hedgehog directs specialised mesoderm differentiation in the intestine and pancreas", Curr. Biol. 7:801-804	
	BA	Armentano et al., 1990, "Expression of human factor IX in rabbit hepatocytes by retrovirus-mediated gene transfer: potential for gene therapy of hemophilia B", Proc. Natl. Acad. Sci. USA 87:6141-6145	
	BB	Barbas et al., 1992, "Semisynthetic combinatorial antibody libraries: a chemical solution to the diversity problem", Proc. Natl. Acad. Sci. USA 89:4457-4461	
	BC	Berkner et al., 1988, "Development of adenovirus vectors for the expression of heterologous genes", Biotechniques 6:616-629	
	BD	Boerner et al., 1991, "Production of antigen-specific human monoclonal antibodies from in vitro-primed human splenocytes", J. Immunol. 147:86-95	
	BE	Breslow, 1996, "Mouse models of atherosclerosis", Science 272:685-688	
	BF	Callow et al., 1994, "Expression of human apolipoprotein B and assembly of lipoprotein(a) in transgenic mice", Proc. Natl. Acad. Sci. USA 91:2130-2134	
	BG	Chang et al., 1994, "Products, genetic linkage and limb patterning activity of a murine hedgehog gene", Development 120:3339-3353	
	BH	Charbit et al., 1986, "Probing the topology of a bacterial membrane protein by genetic insertion of a foreign epitope; expression at the cell surface", EMBO J. 5:3029-3037	
	BI	Chen et al., "Gene therapy for brain tumors: regression of experimental gliomas by adenovirus-mediated gene transfer in vivo", Proc. Natl. Acad. Sci. USA 91:3054-3057	
	BJ	Chowdhury et al. 1991, "Long-term improvement of hypercholesterolemia after ex vivo gene therapy in LDLR-deficient rabbits", Science 254:1802-1805	
	BK	Clackson et al., 1991, "Making antibody fragments using phage display libraries", Nature 352:624-628	
	BL	Co et al., 1991, "Humanized antibodies for antiviral therapy", Proc. Natl. Acad. Sci. USA 88:2869-2873	
W/	BM	Cull et al., 1992, "Screening for receptor ligands using large libraries of peptides linked to the C terminus of the lac repressor", Proc. Natl. Acad. Sci. USA 89:1865-1869	

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WJ	BN	Cunningham and Wells, 1989, "High-resolution epitope mapping of hGH-receptor interactions by alanine-scanning mutagenesis", Science 244:1081-1085	
	BO	Cwirla et al., 1990, "Peptides on phage: a vast library of peptides for identifying ligands", Proc. Natl. Acad. Sci. USA 87:6378-6382	
	BP	Dai et al., 1992, "Gene therapy via primary myoblasts: long-term expression of factor IX protein following transplantation in vivo", Proc. Natl. Acad. Sci. USA 89:10892-10895	
	BQ	Dann et al., 1986, "Human renin: a new class of inhibitors", Biochem. Biophys. Res. Commun. 134:71-77	
	BR	Danos and Mulligan, 1988, "Safe and efficient generation of recombinant retroviruses with amphotropic and ecotropic host ranges", Proc. Natl. Acad. Sci. USA 85:6460-6464	
	BS	Devlin et al., 1990, "Random peptide libraries: a source of specific protein binding molecules", Science 249:404-406	
	BT	Echelard et al., 1993, "Sonic hedgehog, a member of a family of putative signaling molecules, is implicated in the regulation of CNS polarity", Cell 75:1417-1430	
	BU	Eglitis et al., 1985, "Gene expression in mice after high efficiency retroviral-mediated gene transfer", Science 230:1395-1398	
	BV	Ekker et al., 1995, "Patterning activities of vertebrate hedgehog proteins in the developing eye and brain", Curr. Biol. 5:944-955	
	BW	Fan et al., 1995, "Long-range sclerotome induction by sonic hedgehog: direct role of the amino-terminal cleavage product and modulation by the cyclic AMP signaling pathway", Cell 81:457-654	
	BX	Fancy et al., 1996, "New chemistry for the study of multiprotein complexes: the six-histidine tag as a receptor for a protein crosslinking reagent", Chem. Biol. 3:551-559	
	BY	Farese et al., 1995, "Knockout of the mouse apolipoprotein B gene results in embryonic lethality in homozygotes and protection against diet-induced hypercholesterolemia in heterozygotes", Proc. Natl. Acad. Sci. USA 92:1774-1778	
	BZ	Ferry et al., 1991, "Retroviral-mediated gene transfer into hepatocytes in vivo", Proc. Natl. Acad. Sci. USA 88:8377-8381	
↓	CA	Flotte et al., 1993, "Expression of the cystic fibrosis transmembrane conductance regulator from a novel adeno-associated virus promoter", J. Biol. Chem. 268:3781-3790	

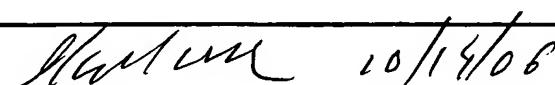
*Glenn* 10/19/08

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WJ	CB	Gordon et al., 1985, "Design of peptide derived amino alcohols as transition-state analog inhibitors of angiotensin converting enzyme", Biochem. Biophys. Res. Commun. 126:419-426		
	CC	Griffiths et al., 1993, "Human anti-self antibodies with high specificity from phage display libraries", EMBO J. 12:725-734		
	CD	Gross and Witkip, 1961, "Selective cleavage of the methionyl peptide bonds in ribonuclease with cyanogen bromide", J. Am. Chem. Soc. 83:1510		
	CE	Hall et al., 1995, "A potential catalytic site revealed by the 1.7-A crystal structure of the amino-terminal signalling domain of Sonic hedgehog", Nature 378:212-216		
	CF	Hansson et al., 1992, "Expression of recombinant proteins on the surface of the coagulase-negative bacterium <i>Staphylococcus xylosus</i> ", J. Bacteriol. 174:4239-4245		
	CG	Hermonat et al., 1984, "Use of adeno-associated virus as a mammalian DNA cloning vector: transduction of neomycin resistance into mammalian tissue culture cells", Proc. Natl. Acad. Sci. USA 81:6466-6470		
	CH	Homanics et al., 1993, "Targeted modification of the apolipoprotein B gene results in hypobetalipoproteinemia and developmental abnormalities in mice", Proc. Natl. Acad. Sci. USA 90:2389-2393		
	CI	Huang and Stoller, 1991, "Construction of representative immunoglobulin variable region cDNA libraries from human peripheral blood lymphocytes without in vitro stimulation", J. Immunol. Methods 141:227-236		
	CJ	Huber et al., 1991, "Retroviral-mediated gene therapy for the treatment of hepatocellular carcinoma: an innovative approach for cancer therapy", Proc. Natl. Acad. Sci. USA 88:8039-8043		
	CK	Hwu et al., 1993, "Functional and molecular characterization of tumor-infiltrating lymphocytes transduced with tumor necrosis factor-alpha cDNA for the gene therapy of cancer in humans", J. Immunol. 150:4104-4115		
	CL	Ike et al., 1983, "Solid phase synthesis of polynucleotides. VIII. Synthesis of mixed oligodeoxyribonucleotides by the phosphotriester solid phase method", Nucleic Acids Res. 11:477-488		
	CM	Itakura et al., 1981, Recombinant DNA, Proc. 3 <sup>rd</sup> Cleveland Symposium On Macromolecules, A.G. Walton, ed. (Elsevier, Amsterdam) pp. 273-289		
	CN	Itakura et al., 1984, "Expression in <i>Escherichia coli</i> of a chemically synthesized gene for the hormone somatostatin", Science 198:1056-1063		
WJ	CO	Itakura et al., 1984, "Synthesis and use of synthetic oligonucleotides", Annu. Rev. Biochem. 53:323-356		

*Markus 10/14/08*

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			Applicant Burkly and Wang	
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✓	CP	Jones et al., 1986, "Replacing the complementarity-determining regions in a human antibody with those from a mouse", Nature 321:522-525		
	CQ	Kaufman and Sharp, 1982, "Construction of a modular dihydrofolate reductase cDNA gene: analysis of signals utilized for efficient expression", Mol. Cell. Biol. 2:1304-1319		
	CR	Kay et al., 1992, "Hepatic gene therapy: persistent expression of human alpha 1-antitrypsin in mice after direct gene delivery in vivo", Hum. Gene Ther. 3:641-647		
	CS	Kinto et al., 1997, "Fibroblasts expressing Sonic hedgehog induce osteoblast differentiation and ectopic bone formation", FEBS Lett. 404:319-323		
	CT	Klauser et al., 1990, "Extracellular transport of cholera toxin B subunit using Neisseria IgA protease beta-domain: conformation-dependent outer membrane translocation", EMBO J. 9:1991-1999		
	CU	Kohler et al., 1975, "Continuous cultures of fused cells secreting antibody of predefined specificity", Nature 256:495-497		
	CV	Kuwajima et al., 1988, "Presentation of an antigenic determinant from hen egg-white lysozyme on the flagellar filament of Escherichia coli", Bio/Tech. 6:1080-1083		
	CW	Leung et al., 1989, "A method for random mutagenesis of a defined DNA segment using a modified polymerase chain reaction", Technique 1:11-15		
	CX	Lindley, 1956, "A new synthetic substrate for trypsin and its application to the determination of the amino-acid sequence of proteins", Nature 178:647		
	CY	Linton et al., 1993, "Familial hypobetalipoproteinemia", J. Lipid Res. 34:521-541		
	CZ	Litingtung et al., 1998, "Sonic hedgehog is essential to foregut development", Nat. Genet. 20:58-61		
	DA	Mark et al, 1984, "Site-specific mutagenesis of the human fibroblast interferon gene", Proc. Natl. Acad. Sci. USA 81:5662-5666		
	DB	Marks et al., 1992, "Molecular evolution of proteins on filamentous phage. Mimicking the strategy of the immune system", J. Biol. Chem. 267:16007-16010		
	DC	McCormick et al., 1996, "Transgenic mice that overexpress mouse apolipoprotein B. Evidence that the DNA sequences controlling intestinal expression of the apolipoprotein B gene are distant from the structural gene", J. Biol. Chem. 271:11963-11970		
✓	DD	Merrifield, 1967, "New approaches to the chemical synthesis of peptides", Recent Prog. Horm. Res. 23:451-482		

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W	DE	Miller, 1990, "Progress toward human gene therapy", Blood 76:271-278		
	DF	Mohler and Vani, 1992, "Molecular organization and embryonic expression of the hedgehog gene involved in cell-cell communication in segmental patterning of Drosophila", Development 115:957-971		
	DG	Muzychka et al., 1992, "Use of adeno-associated virus as a general transduction vector for mammalian cells", Curr. Top. Microbiol. Immunol. 158:97-129		
	DH	Myers et al., 1985, "A general method for saturation mutagenesis of cloned DNA fragments", Science 229:242-247		
	DI	Narang, 1983, "DNA synthesis", Tetrahedron 39:3-22		
	DJ	Needleman et al., 1970, "A general method applicable to the search for similarities in the amino acid sequence of two proteins", J. Mol. Biol. 48:443-453		
	DK	Orlandi et al., 1989, "Cloning immunoglobulin variable domains for expression by the polymerase chain reaction", Proc. Natl. Acad. Sci. USA 86:3833-3837		
	DL	Persson et al., 1991, "Generation of diverse high-affinity human monoclonal antibodies by repertoire cloning", Proc. Natl. Acad. Sci. USA 88:2432-2436		
	DM	Powell-Braxton et al., 1998, "A mouse model of human familial hypercholesterolemia: markedly elevated low density lipoprotein cholesterol levels and severe atherosclerosis on a low-fat chow diet", Nat. Med. 4:934-938		
	DN	Purcell-Huynh et al., 1995, "Transgenic mice expressing high levels of human apolipoprotein B develop severe atherosclerotic lesions in response to a high-fat diet", J. Clin. Invest. 9:2246-2257 PMID: 7738190		
	DO	Queen et al., 1989, "A humanized antibody that binds to the interleukin 2 receptor", Proc. Natl. Acad. Sci. USA 86:10029-10033		
	DP	Riechmann et al., 1988, "Reshaping human antibodies for therapy", Nature 332:323-327		
	DQ	Roberts et al., 1992, "Directed evolution of a protein: selection of potent neutrophil elastase inhibitors displayed on M13 fusion phage", Proc. Natl. Acad. Sci. USA 89:2429-2433		
	DR	Rosenfeld et al., 1991, "Adenovirus-mediated transfer of a recombinant alpha 1-antitrypsin gene to the lung epithelium in vivo", Science 252:431-434		
↓	DS	Rosenfeld et al., 1992, "In vivo transfer of the human cystic fibrosis transmembrane conductance regulator gene to the airway epithelium", Cell 68:143-155		



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WY	DT	Sato et al., 1986, "Synthesis and antibiotic activity of a gramicidin s analogue containing bicyclic beta-turn dipeptides", J. Chem. Soc. Perkin Trans. 1:1231	
	DU	Schorr et al., 1991, "Surface expression of malarial antigens in <i>Salmonella typhimurium</i> : induction of serum antibody response upon oral vaccination of mice", Vaccine 9:675-681	
	DV	Scott et al., 1990, "Searching for peptide ligands with an epitope library", Science 249:386-390	
	DW	Scully et al., 1992, Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 35-1992. An eight-month-old boy with diarrhea and failure to thrive. N. Engl. J. Med. 327:628-635	
	DX	Taylor and Jones, 1979, "Multiple new phenotypes induced in 10T1/2 and 3T3 cells treated with 5-azacytidine", Cell 17:771-779	
	DY	Tempest, 1991, "Reshaping a human monoclonal antibody to inhibit human respiratory syncytial virus infection in vivo", Biotechnology (N Y) 9:266-271	
	DZ	Thiry et al., 1989, "Cloning of DNA sequences encoding foreign peptides and their expression in the K88 pili", Appl. Environ. Microbiol. 55:984-993	
	EA	Tratschin et al., 1984, "A human parvovirus, adeno-associated virus, as a eucaryotic vector: transient expression and encapsidation of the procaryotic gene for chloramphenicol acetyltransferase", Mol. Cell. Biol. 4:2072-2081	
	EB	Van Beusechem et al., 1992, "Long-term expression of human adenosine deaminase in rhesus monkeys transplanted with retrovirus-infected bone-marrow cells", Proc. Natl. Acad. Sci. USA 89:7640-7644	
	EC	Verhoeyen et al., 1988, "Reshaping human antibodies: grafting an antilysozyme activity", Science 239:1534-1536	
	ED	Wang et al., 1993, "Bone morphogenetic protein-2 causes commitment and differentiation in C3H10T1/2 and 3T3 cells", Growth Factors 9:57-71.	
	EE	Wells et al., 1985, "Cassette mutagenesis: an efficient method for generation of multiple mutations at defined sites", Gene 34:315-323	
	EF	Wilson et al., 1988, "Retrovirus-mediated transduction of adult hepatocytes", Proc. Natl. Acad. Sci. USA 85:3014-3018	
	EG	Wondisford et al., 1988, "Cloning of the human thyrotropin beta-subunit gene and transient expression of biologically active human thyrotropin after gene transfection", Mol. Endocrinol. 2:32-9	
↓	EH	Yang et al., 1997, "Expression of human GLI in mice results in failure to thrive, early death, and patchy Hirschsprung-like gastrointestinal dilatation", Mol. Med. 3:826-835	

*Markus 10/18/06*

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W	EI	Young et al, 1995, "A genetic model for absent chylomicron formation: mice producing apolipoprotein B in the liver, but not in the intestine", J. Clin. Invest 96:2932-2946		
	EJ	Incardona et al., "The Teratogenic Veratrum Alkaloid Cyclopamine Inhibits Sonic Hedgehog Signal Transduction," Development 125:3553-3562 (1998)		
	EK	Bowie et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," Science 247:1306-1310 (1990)		
↓	EL	Chiang et al., "Cyclopia and Defective Axial Patterning in Mice Lacking Sonic Hedgehog Gene Function," Nature 383:407-413 (1996)		
EXAMINER	<i>Mark</i>		DATE CONSIDERED 10/14/06	
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